FDA Adverse Event Reporting System (FAERS) reporting and review
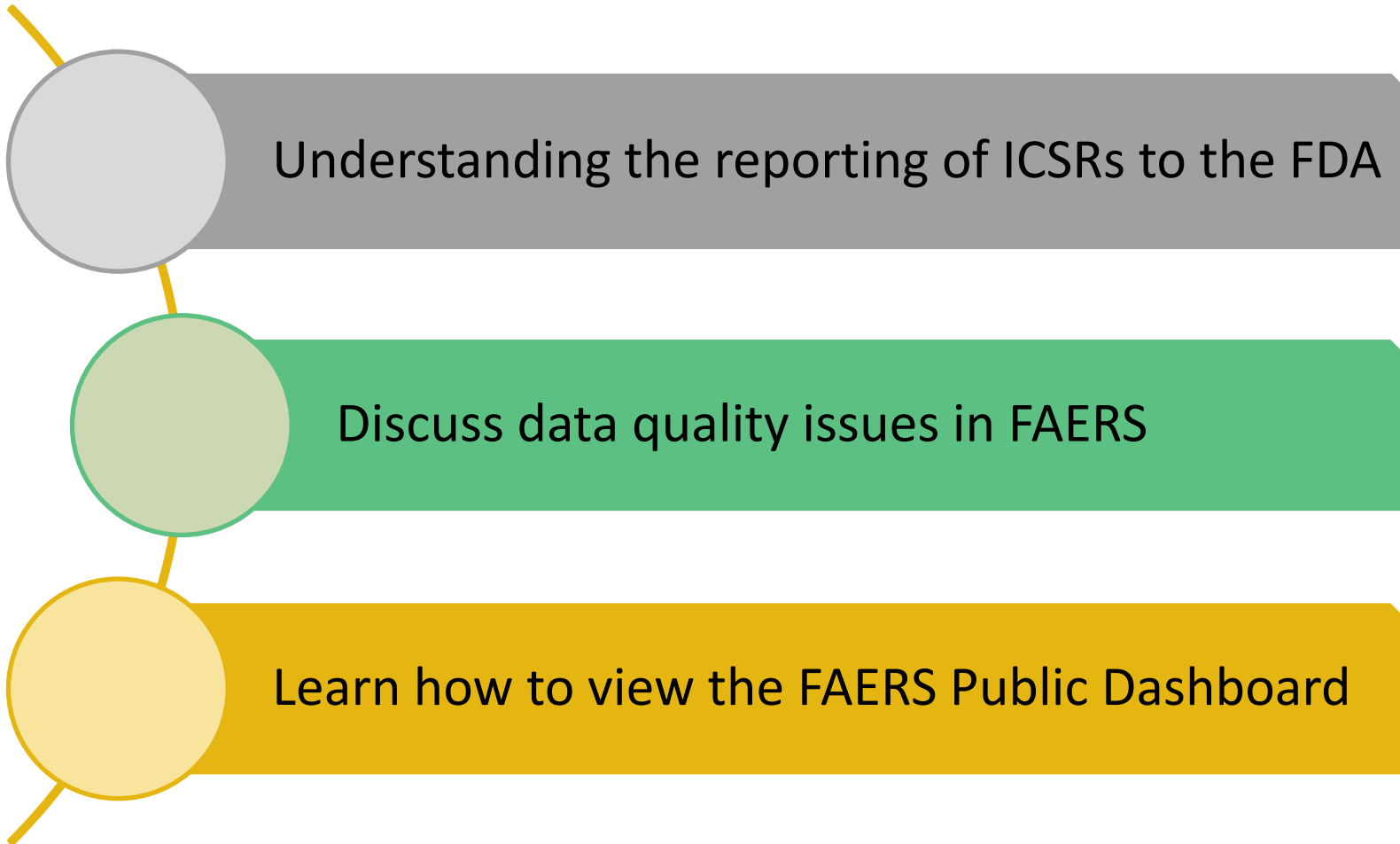
Suranjan De, MS, MBA

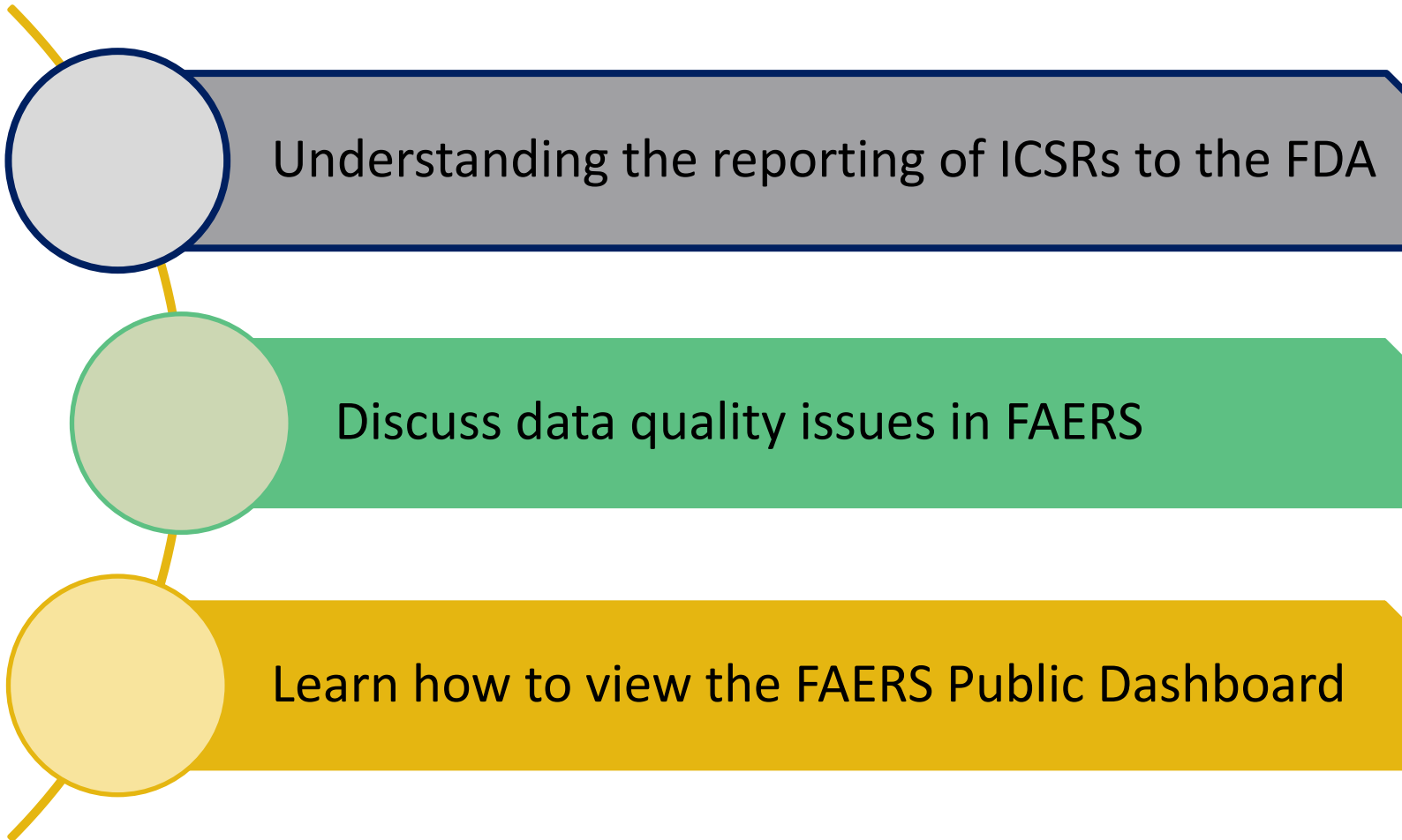CDER/OSE/RSS

Disclaimer

FDA

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Learning Objectives

Understanding the reporting of ICSRs to the FDA

Discuss data quality issues in FAERS

Learn how to view the FAERS Public Dashboard

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FDA Adverse Event Reporting System (FAERS)

The FDA Adverse Events Reporting System (FAERS) is a database that contains **spontaneous adverse event reports** that are **submitted to FDA** by the **product manufacturer or directly from the consumer, healthcare professional, or other reporter**. The database supports the FDA's post marketing safety surveillance program for **drug and therapeutic biological products**.

The database consists of more than **twenty-four (24) million reports** since 1969 to March 2022. Each year, FDA receives **over two (2) million** adverse events and medication error reports associated with the use of drug or biologic products.

FDA modernized the FAERS system in Nov 2021

FDA Adverse Event Reporting System

FDA's postmarketing safety surveillance database for **drugs and therapeutic biologics**

FDA uses FAERS data to **monitor, identify and analyze adverse event and medication errors**
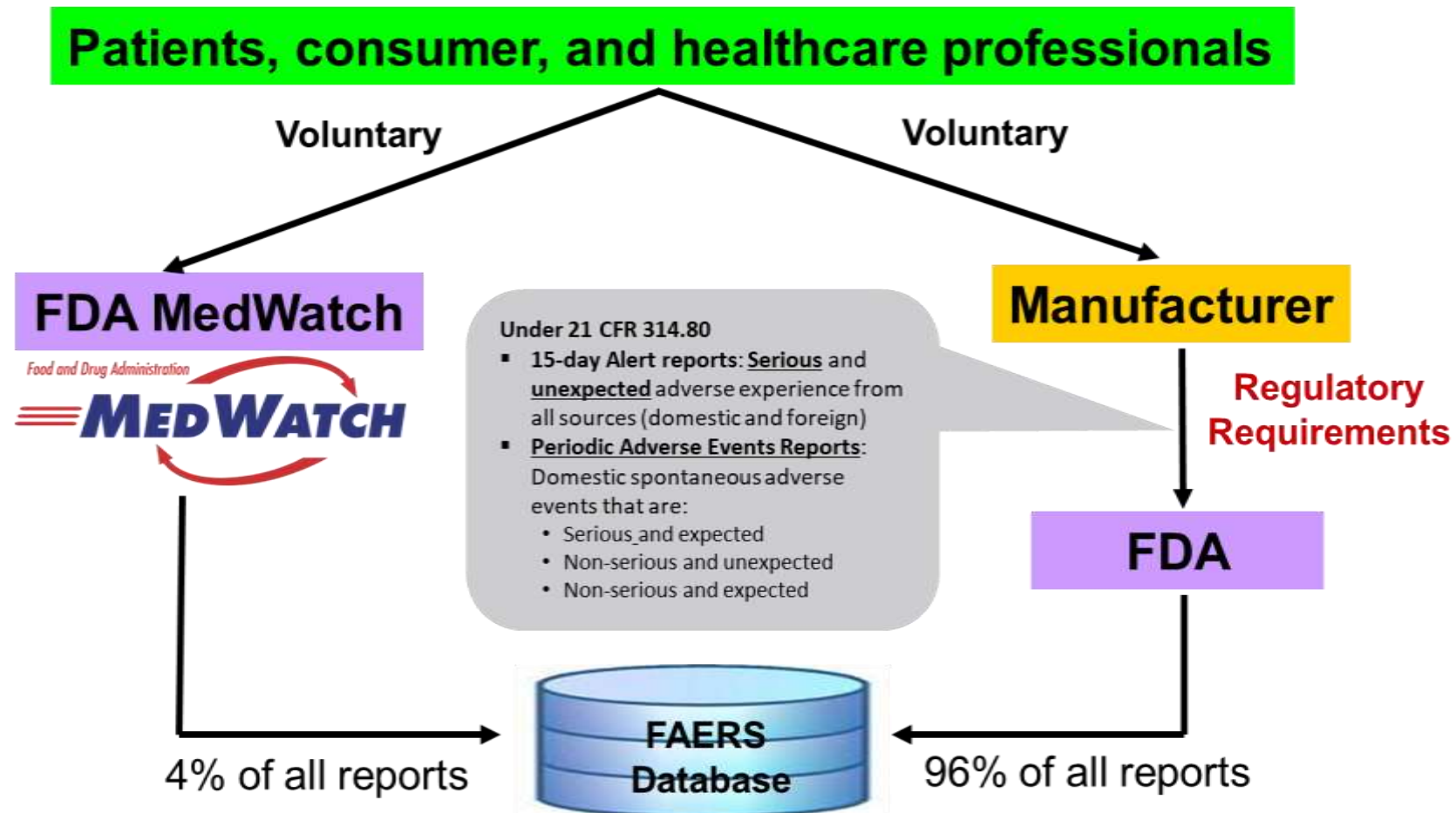
FDA staff in CDER and CBER **regularly examine** the FAERS database as part of **routine safety monitoring**

When a **safety signal is identified** from FAERS data, it is further evaluated

How post-marketing adverse event reports get to FDA

Serious Adverse Event

- Results in any of these outcomes:
  - ❏ Death
  - ❏ Life-threatening adverse experience
  - ❏ Inpatient hospitalization – new or prolonged
  - ❏ Persistent/significant disability or incapacity
  - ❏ Congenital birth defect
  - ❏ Other serious: based upon appropriate medical judgment, these AEs may jeopardize the patient and require intervention to prevent a serious outcome

Federal Register - Code of Federal Regulations. **21 CFR 314.80** *(a)*

What Reports are in the FAERS Database?

FDA

Medication Errors

Adverse Events

Product Problem (with AE)

FAERS

For

Drugs and therapeutic biologics (Rx + OTC) - CDER

Tissue products, therapeutic blood products - CBER

Source of Reports in FAERS

- Adverse event reporting is a **voluntary process** for healthcare professionals in the U.S.

- Healthcare professionals and consumers may send reports to **manufacturers and/or the FDA** (spontaneous reporting)

- Manufacturers are **required to forward reports** to FDA as per regulation

- Manufacturers have **additional reporting requirements**, such as post-marketing study reports

Electronic Reporting of ICSRs

Submit safety reports in an electronic format that FDA can process, review, and archive

Improve the Agency's systems for **collecting and analyzing** postmarketing safety reports

Enable Agency to **more rapidly review** postmarketing safety reports, **identify and evaluate** emerging safety problems, and **disseminate** safety information in support of FDA's public health mission

Electronic submission of ICSRs **enhances** global pharmacovigilance by **facilitating electronic transmission and exchange of appropriate information** from ICSRs among regulatory bodies and regulated entities through use of **common data elements and transmission standards**

Electronic Reporting of ICSRs

FDA

Submission Methods

• There are two options for submitting ICSRs electronically

> • **The Safety Reporting Portal (SRP) by manually entering data via web form**
>   • Do not have database-to-database capability
>   • Must have an account to access the portal site
>   • Gateway partners cannot use the SRP
>   • Attachments must be in the PDF format

Safety Reporting Portal

E2B R2

E2B R2

Acknowledgement

FDA ESG

FAERS

Industry

> • **Database-to-database transmission ("E2B")**
>   • Use standardized ICH E2B(M) data elements
>   • ICSRs must be submitted in the XML format
>   • Attachments must be in the PDF format

Safety Reporting Portal (SRP)

Safety Reporting Portal (SRP)

- SRP is based on the data elements from the MedWatch 3500A

To register send request email to: faersesub@fda.hhs.gov

Electronic Reporting of ICSRs

Submitting Periodic Safety Reports (PSR)

Periodic safety reports are comprised of a **descriptive portion** and **non-expedited ICSRs** (21 CFR 314.80 and 600.80), regardless of the format.

- **Descriptive Portion:**

  - Use **Electronic Common Technical Document (eCTD)** specifications to submit the descriptive portion electronically.

  - **Indicate** in the descriptive portion that the **ICSRs have been submitted electronically** as XML files to the FDA Electronic Submissions Gateway (ESG) or via the Safety Reporting Portal (SRP).

- **Non-expedited ICSRs:** must be submitted as described in the options **on or before** the periodic safety report due date. Do NOT submit expedited ICSRs previously submitted.

FAERS Electronic Submissions

Premarketing Safety Reporting

In preparation for the electronic transmission of premarketing safety reports in the International Council for Harmonisation (ICH) E2B(R3) format, FDA has posted the following documents regarding the electronic submission of ICSRs for certain investigational new drug application (IND) safety reports for drug and biological products, to FAERS. These documents are posted to help sponsors prepare their systems for electronic submission of IND safety reports in the E2B(R3) format.

1. Providing Regulatory Submissions in Electronic Format: IND Safety Reports - Draft Guidance for Industry (October 2019)

2. Electronic Submission of IND Safety Reports - Technical Conformance Guide (April 2022)

3. Technical Specifications Document - FDA Regional Implementation Guide for E2B(R3) Electronic Transmission of Individual Case Safety Reports for Drug and Biological Products (April 2022)

4. FDA E2B(R3) Core and Regional Data Elements and Business Rules (Excel file April 2022)

5. FDA ICSR XML Instances (zip file April 2022)

Please note, FDA is not currently accepting the submission of premarket ICSRs in the E2B(R3) format. Please continue to submit IND Safety Reports using eCTD format. FDA will update this web page when final guidance is published, and when FDA will accept IND and IND-exempt bioavailability/bioequivalence (BA/BE) safety reports in E2B(R3) format on a voluntary basis. FDA will also update this web page to communicate when submission of safety reports in E2B(R3) format is required for certain IND and IND-exempt BA/BE studies, after the period of voluntary submission.

https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions

FAERS Electronic Submissions

Postmarketing Safety Reporting

In preparation for the receipt of postmarketing safety reports in the E2B(R3) format, FDA has posted the following documents regarding the electronic submission of safety reports for drug and biological products to FAERS. These documents are posted to help prepare systems for electronic submissions of postmarketing safety reports.

1. Technical Specifications Document - FDA Regional Implementation Guide for E2B(R3) Electronic Transmission of Individual Case Safety Reports for Drug and Biological Products (April 2022)

2. FDA E2B(R3) Core and Regional Data Elements and Business Rules (Excel file April 2022)

3. FDA E2B(R3) Forward Compatible Rules (Excel file April 2022)

4. FDA ICSR XML Instances (zip file April 2022)

5. Providing Submissions in Electronic Format – Postmarketing Safety Reports: Guidance for Industry (April 2022)

Please note, FDA is not currently accepting the submission of postmarketing ICSRs in the E2B(R3) format. FDA will update this web page when postmarketing ICSRs will be accepted in the E2B(R3) format. In the meantime, please continue to submit postmarketing ICSRs in the E2B(R2) format.

For questions related to this update, please contact the FAERS electronic submission coordinator at faersesub@fda.hhs.gov.

https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions

FAERS Report Volume

Last 10 years
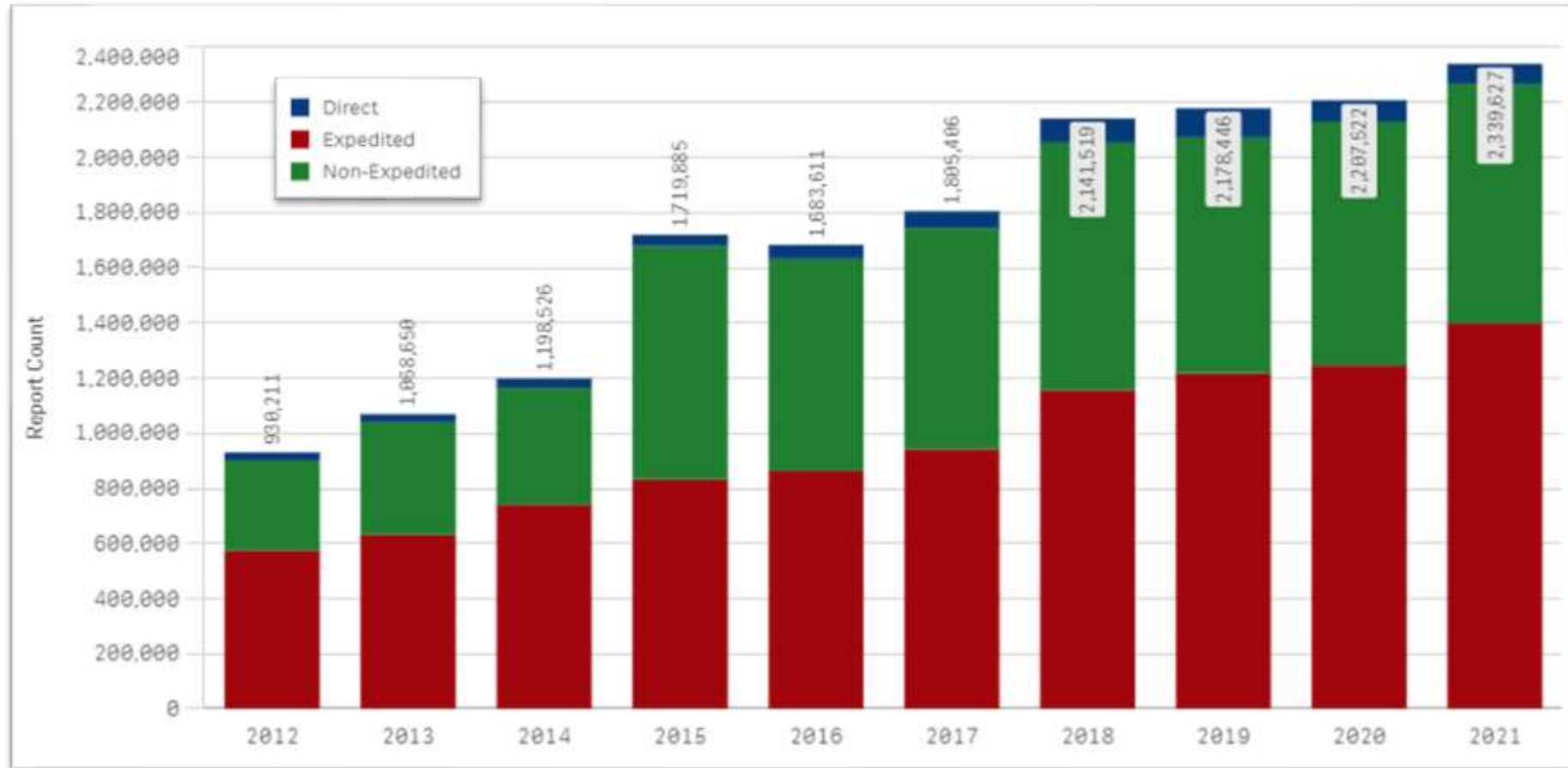
Source: FAERS Public Dashboard

Processing of Adverse Event Reports

Factors Affecting Reporting

- Media attention
- Litigation (class action lawsuits)
- Nature of the adverse event
- Type of drug product and indication
- Length of time on market
- Extent and quality of surveillance system
- Prescription or OTC product status
- Reporting regulations
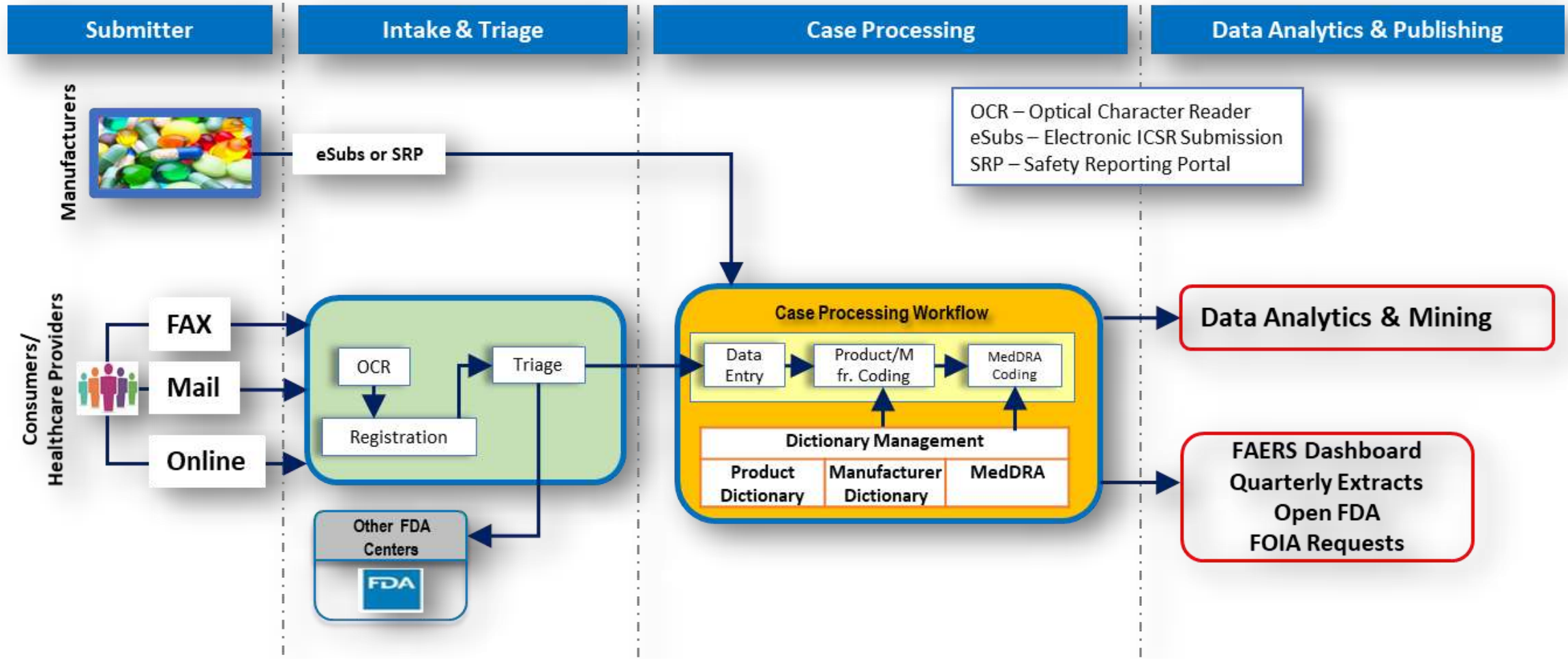
Electronic Submission References

Reference Area	Reference Link
FAERS Electronic Submission (eSub)	https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-electronic-submissions
Electronic submission inquiries	faersesub@fda.hhs.gov
Electronic Submission Gateway (ESG)	https://www.fda.gov/industry/electronic-submissions-gateway
Electronic Submission Gateway inquiries	ESGHelpDesk@fda.hhs.gov
Providing Submission in Electronic Format – Postmarketing Safety Reports	https://www.fda.gov/regulatory-information/search-fda-guidance-documents/providing-submissions-electronic-format-postmarketing-safety-reports

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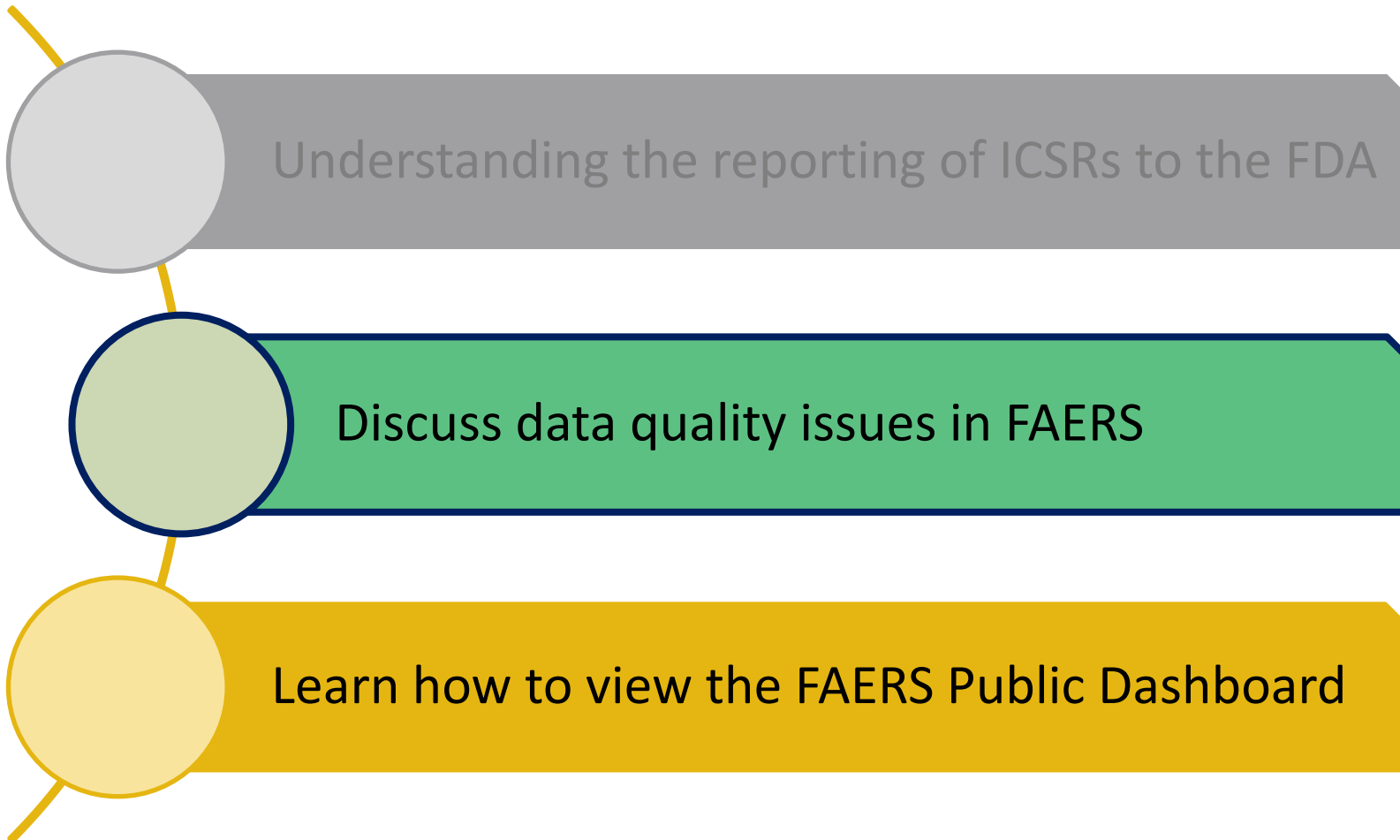
Topics Covered

- Issues with reported suspect products and recommendations

- Other data issues

Main Data Sources for Product Validation in FAERS

- **Substance Registration System (SRS) for all products**
  - 'Preferred name' for active ingredient, active moiety
  - SRS public database (NLM): https://fdasis.nlm.nih.gov/srs/

- **Structured Product Labeling (SPL) for US marketed products**
  - Product name with active ingredient and moiety from SRS

- **Non-US marketed products**
  - Product information: WHODrug Global
  - Active ingredient: SRS Preferred name

- **Other validated sources**

Issues with Reported Suspect Products

FDA

Two products reported as one multi-ingredient product (which does not exist as a single formulation):

- *"IPILIMUMAB/NIVOLUMAB"*
- *"SULFAMETHOXAZOLE\TRIMIPRAMINE"*
- *"EPIRUBICIN/VINORELBINE*

Recommend to separate suspect products that do not exist as a single multi-ingredient formulation.

Issues with Reported Suspect Product

Two product names reported for the first suspect product in the MedWatch Form

- Example:
  - PRODUCT X and PRODUCT Y

Recommend to report one product name per each line in the MedWatch Form.

If brand/trade name is unknown and reporting a product with multi active ingredients, then report as

D. SUSPECT PRODUCTS

1. **Name, Strength, Manufacturer/Compounder** *(from product label).*
Does this report involve cosmetic, dietary supplement or food/medical food? #1 ☐ Yes / #2 ☐ Yes

#1 – Name and Strength	#1 – NDC # or Unique ID
PRODUCT X	
#1 – Manufacturer/Compounder	#1 – Lot #
#2 – Name and Strength	#2 – NDC # or Unique ID
PRODUCT Y	
#2 – Manufacturer/Compounder	#2 – Lot #

D. SUSPECT PRODUCTS

1. **Name, Strength, Manufacturer/Compounder** *(from product label).*
Does this report involve cosmetic, dietary supplement or food/medical food? #1 ☐ Yes / #2 ☐ Yes

#1 – Name and Strength	#1 – NDC # or Unique ID
INGREDIENT 1\INGREDIENT 2	
#1 – Manufacturer/Compounder	#1 – Lot #
#2 – Name and Strength	#2 – NDC # or Unique ID
#2 – Manufacturer/Compounder	#2 – Lot #

Issues with Reported Suspect Product

Narrative and structured field(s) do not match

- Ingredient salt stated in narrative, structured field populated with a different salt form
  - Narrative: "…received Pseudoephedrine hydrochloride"
  - Structured field: "Pseudoephedrine hydrobromide"

- Inconsistency
  - Narrative: "…given treatment of INETETAMAB"
  - Substance name in structured field: "INOTUZUMAB"

- Report the product name as mentioned in the label

Issues with Reported Suspect Product

Non-unique product name with different active ingredients

ACIDEX

ICY HOT

Recommend to append the active ingredient to the reported drug name. For example,

ACIDEX [OMEPRAZOLE]
ACIDEX [RANITIDINE HYDROCHLORIDE]
CLAMISIN [CLARITHROMYCIN]
CLAMISIN [TERBINAFINE]

Other Data Issues

❑ Some product information reported without product name

❑ Application number incorrectly or not reported for the Company's product

❑ Information in narrative but not in structured data elements (e.g., demographics data)

❑ Demographic information incomplete or off limits

❑ Information not presented correctly via structured data elements (e.g., abated and reappeared)

❑ Outcome inappropriately documented

❑ Date mismatch (e.g., event date prior to therapy date)

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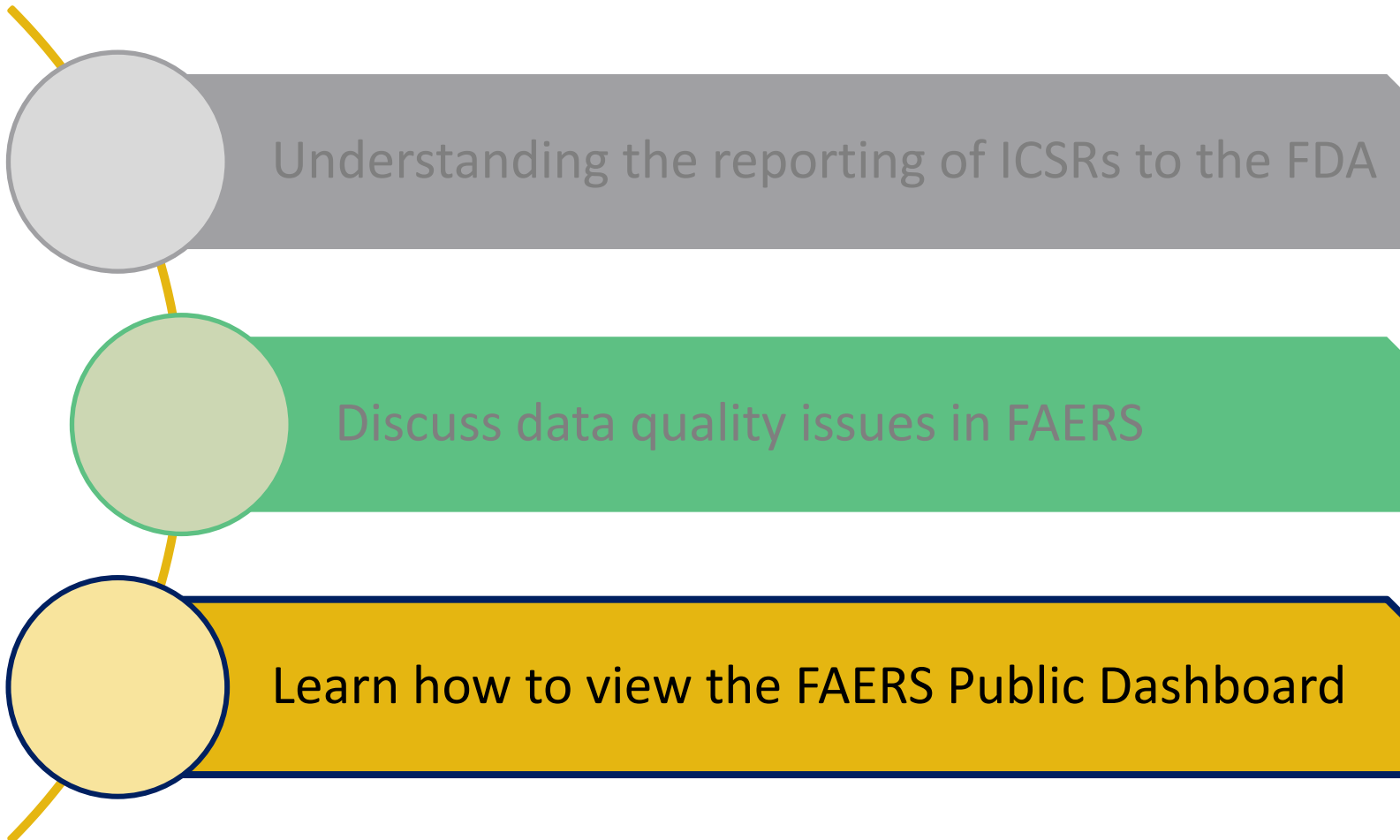
Topics Covered

- Describe the FAERS public database

- Demonstrate how view adverse event reporting metrics

- Illustrate viewing of adverse event information

FAERS Public Dashboard

FDA provides information to the public in an accessible and transparent manner. FAERS dashboard gives the public and industry a more **user friendly platform** for accessing FAERS reports and making adverse event data more **accessible and transparent**.

FAERS data outlets for public:

JSON File(s)

Text/ASCII Files and XML File(s)

Easy Interactive Access

Open FDA

FAERS Quarterly Data Extracts (QDE)

FAERS Public Dashboard

The FAERS Public Dashboard is an **interactive application**, which enables the user to search for information related to adverse events reported to the FDA by the pharmaceutical industry, healthcare providers and consumers.

Key Points to Consider

❑ **Data Quality**
  ▪ There are many instances of duplicative reports and some reports do not contain all the necessary information.

❑ **Existence of a report does not establish causation**
  ▪ There is no certainty that a suspected drug caused the adverse events.
  ▪ Adverse events may have been related to the underlying disease being treated, or caused by some other drug being taken concurrently, or occurred for other reasons.
  ▪ The information in these reports reflects only the reporter's observations and opinions.

❑ **Information in reports has not been verified**
  ▪ Submission of a report does not mean that the information included in it has been medically confirmed.

Key Points to Consider

❑ **Rates of occurrence cannot be established with reports**
- ▪ The number of adverse events should not be used to determine the likelihood of a side effect occurring.
- ▪ Factors such as the time a product has been marketed and publicity can influence reporting.

❑**Patients should talk to their doctor** before stopping or changing how they take their medications

❑**Patient Outcomes received in FAERS**
- ▪ A reported serious outcomes does not necessarily mean that the suspect product(s) named in the report was the cause of these outcomes.

To request individual case reports, submit FOIA request with a listing of case report numbers.
(https://www.fda.gov/drugs/questions-and-answers-fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-latest-quarterly-data-files#FOIA)

Launch FAERS Public Dashboard

https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/ucm070093.htm

FDA FDA Adverse Event Reporting Sy ×   Q FDA Adverse Events Reporting S; ×   +

← → C   🔒 fis.fda.gov/sense/app/95239e26-e0be-42d9-a960-9a5f7f1c25ee/sheet/7a47a261-d58b-4203-a8aa-6d3021737452/state/analysis

⊞ Apps   ⊙ LSMV   🐦 Insight   G Google   🏃 ICH Templates | ICH...   ⊙ LSMV Prod   ⊙ lsmv-rapid.dev.fda...   📧 LSMV E2B Validator   📧 RxLogix Dashboard   ⊙ New Tab   🧰 Home - Commuter...   🔵 eCORP   📧 RxLogix Preprod   »

No selections applied

FDA Adverse Events Reportin   **FDA** **U.S. FOOD & DRUG**
ADMINISTRATION

Home   Q Search   COVID-19 EUA   Report a Problem   FAQ   Site Feedback

Disclaimer

Each year, the FDA receives over one million adverse event and medication error reports associated with the use of drug or biologic products. The FDA uses these reports to monitor the safety of drug and biological products. The FDA Adverse Event Reporting System (FAERS) database houses reports submitted to the FDA by drug manufacturers (who are required to submit these reports to FDA) and others such as health care professionals and consumers. Submission of a safety report does not constitute an admission that medical personnel, user facility, importer, distributor, manufacturer or product caused or contributed to the event.

Although these reports are a valuable source of information, this surveillance system has limitations, including the potential submission of incomplete, inaccurate, untimely and/or unverified information. In addition, the incidence or prevalence of an event cannot be determined from this reporting system alone due to potential under-reporting of events and lack of information about frequency of use. Because of this, FAERS data comprise only one part of the FDA's important post-market surveillance data and the information on this website does not confirm a causal relationship between the drug product and the reported adverse event(s).

- Consumers should not stop or change medication without first consulting with a health care professional.
- The FAERS web search feature is limited to adverse event reports between 1969 and the most recent quarter for which data are available.
- Data submitted to the FAERS system will be made available through the new querying tool on a quarterly basis.
- FAERS data alone cannot be used to establish rates of events, evaluate a change in event rates over time or compare event rates between drug products. The number of reports cannot be interpreted or used in isolation to reach conclusions about the existence, severity, or frequency of problems associated with drug products.
- Confirming whether a drug product actually caused a specific event can be difficult based solely on information provided in a given report.
- FAERS data do not represent all known safety information for a reported drug product and should be interpreted in the context of other available information when making drug-related or treatment decisions.
- Variations in trade, product, and company names affect search results. Searches only retrieve records that contain the search term(s) provided by the requester.

Importantly, safety reports submitted to FDA do not necessarily reflect a conclusion by FDA that the information in the reports constitutes an admission that the drug caused or contributed to an adverse event. Individual FAERS reports for a given product can be requested by submitting a Freedom of Information Act (FOIA) request at:
https://www.fda.gov/regulatoryinformation/foi/howtomakeafoiarequest/default.htm

Challenge Question# 1

What are the submission methods?

a. MedWatch Online

b. Safety Reporting Portal

c. Electronic Submission Gateway

d. b and c

Challenge Question# 2

Typical data issues encountered in a safety report submission

a. Information in narrative but not in structured data elements

b. Demographic information incomplete or off limits

c. Product name mismatch or inconsistency

d. Date mismatch

e. All of the above

Challenge Question# 3

A manufacturer is searching for reports on their product. Select the applicable options to perform this search?

a. By NDA number

b. By Brand Name

c. By Generic Name

d. By Brand Name or Generic Name

e. None of the above

Thank You